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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/715,776	11/18/2003	Lee E. Goldstein	27374-006 CIP	4569

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EXAMINER	
SAMALA, JAGADISHWAR RAO	
ART UNIT	**PAPER NUMBER**
1618	

DATE MAILED: 11/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/715,776	GOLDSTEIN ET AL.	
	Examiner	Art Unit	
	Jagadishwar R. Samala	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-11 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-11 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 12/18/03.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election Acknowledged

1. Applicant's election with partial traverse the invention group I of claims 1-11 and election of species Thioflavin is acknowledged.

And the invention for group II, III and IV will not be included to examine.

Claim Disposition

2. Claims 1-11 is pending and will be presented for examination.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1,4-11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a detectably-labeled compound that binds to an amyloid protein is a fluorescent dye, does not reasonably provide enablement for any fluorescent dye to bind to an amyloid protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Accordingly, the examiner purports that it would constitute undue experimentation to determine what compounds or fluorescent dyes can be effectively employed as a detectably-labeled compounds as per the parameters of the instant claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above factors are weighed, it is examiner's position that one skilled in the art could not practice the invention without undue experimentation.

(1) Nature of the Invention.

The claims are drawn to method of diagnosing Alzheimer's disease comprising contacting an ocular tissue with a detectably-labeled compound like fluorescent dye that binds to an amyloid protein.

(2) The state of art.

The state of prior art concerning the use of radioactively labeled compound of similar mode of action to treat or prevent amyloid disease is well recognized. However, the state of art concerning the use of detectably-labeled compounds such as fluorescent dye to bind to an amyloid protein is not well recognized as there are numerous detectably-labeled compounds which binds to an amyloid-protein and quantitating the level of association of the compound with amyloid protein (ocular tissue). Until this time, there has been no useful method of diagnosing Alzheimer's disease. The existence of a detectably-labeled compound such as fluorescent dye is contrary to our present

understanding of oncology. Thus, it is beyond the skilled artisan today to get a detectably-labeled compound such as a radioactively labeled fluorescent dye to be an effective against amyloid protein, which indicates that said mammal is suffering from or is at risk of developing Alzheimer's disease.

(3) The relative skill of those in the art

The relative skill of those in the art of pharmaceuticals is high. As seen in Klunk et al., (WO 02/16333) which discloses the method of using the thioflavin derivatives in the diagnosis and treatment of patients having diseases where accumulation of neuritic plaques are prevalent. Glenner et al.,(US 4,666,829) discloses a novel polypeptide, which can be used to obtain antibodies to recognize antigenic determinants of the polypeptide or homologous polypeptides in tissues or body fluids as a specific immunologic diagnostic test for Alzheimer's disease.

(4) The predictability or unpredictability of the art.

The art pertaining to diagnosing Alzheimer's disease using detectably-labeled compounds such as fluorescent dye is highly unpredictably, due to binding of the compound to the ocular tissue, as compared to the level of binding in a normal control tissue would be effectively treated thereby. Pharmacological activity of the radiolabeled compound in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, the "scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved".

(5) The breadth of the claims

The instant claims embrace to a method of diagnosing Alzheimer's disease comprising contacting an ocular tissue with a detectably-labeled compound that binds to an amyloid protein. The instant claims cover "Amyloid Disease" that is known to exist for which there is no enablement provided.

The claims are broad as the recitation of "fluorescent dye" encompasses a vast number of fluorescent dyes with a vast number of compounds and different physiology.

(6) The amount of direction or guidance presented.

The instant disclosure provides guidance through the examples and the disclosure of the sufficient direction for the use of certain detectably-labeled compounds. Although the specification and disclosure provide enabling disclosure for using certain fluorescent compounds as effective binding agents to amyloid protein, none of the specification or the disclosure provides enabling disclosure for using detectably-labeled compounds to bind to amyloid protein as claimed and there is insufficient evidence for the claimed use of fluorescent dye as an effective binding agent to amyloid protein, wherein an increase in binding of said compound to ocular tissue compared to a normal control level of binding leads to diagnosis of Alzheimer's disease. The specification provides no guidance, in the way of enablement for the full scope of fluorescent compounds that are potentially suitable for the invention work similarly as to amyloid protein binding agents. The skill artisan would have not known that which fluorescent dye of the claimed compounds are capable of accomplishing the desired result of the claimed invention without undue amount of experiments.

(7) The presence or absence of working examples

As stated above, the specification and disclosure only provide the usefulness of detectably-labeled compound in diagnosis of amyloidotic diseases. Both specification and the disclosure fail to provide adequate representation regarding the conclusion of the efficacy of detectably-labeled compound in treating or screening (diagnosis) amyloid protein assembly into insoluble fibrils which, in vivo are deposited in various organs.

(8) The quantity of experimentation necessary

Since the efficacy of detectably-labeled compound such as fluorescent dye in preventing or inhibiting amyloid protein assembly mentioned above cannot be predicted from a priori but must be determined from the case to case by painstaking experimental study and when the above factors are weighed together, one of ordinary skill in the art would be burdened with undue " painstaking experimentation study" to use the invention commensurate in scope with the claims.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Klunk et al., (US 2002/0133019 here after '019) view of Potter (US 5,571,671 here after '671).

Klunk discloses the method of using the thioflavin derivatives, in the diagnosis and treatment of patients having diseases where accumulation of neuritic plaques are prevalent in AD by vivo imaging of patients having neuritic plaques (see abstract).

Klunk fails to disclose the use of thioflavin derivatives as detectably-labeled compounds that binds to ocular tissue. However, the use of radioactively labeled compound a fluorescent dye that binds to an amyloid protein is well known in the art as shown by Potter.

Potter discloses a method for detecting Alzheimer's disease comprising testing an individual for the presence of a mosaic population of cells (indicative of Alzheimer's disease) in which some cells have two copies of chromosome 21 and some cells have three copies of chromosome 21 (see abstract)

It would have been obvious to one of ordinary skill in the art to modify the thioflavin derivatives disclosed by Klunk as detectably-labeled compound that bind to ocular tissue because Potter teaches that, that thioflavin S, a histological marker for amyloid, showed positive staining within a few cells and around some blood vessels. Additionally thioflavin S effectively binds to antisera to the β-protein precursor, to β-protein itself, to ACT, to PHF, and to phosphorylated epitopes of tau labeled a few percent of cells in the trisomy 16 grafts. One of ordinary skill in the art would have been motivated to include the thioflavin derivatives as a fluorescent dye that binds to an amyloid protein by contacting ocular tissue effectively compared to a normal control level of binding disclosed by Klunk because the thioflavin S , a histological marker for amyloid protein taught by Potter, while having a similar effect as a detectably-labeled

compound that binds to an amyloid protein, provides an additional and separate advantage as compared to the binding agent disclosed by Klunk.

Double Patenting

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1 and 4-11 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 7-16 of U.S. Patent No. 6,849,249. Although the conflicting claims are not identical, they are not patentably distinct from each other because each are drawn to a method of diagnosing Alzheimer's Disease in a mammal by contacting an ocular tissue with a detectably-labeled compound, which binds to an amyloid protein with only slightly differences in describing the functionalities

of the components. For the most part, the patented claims are within the scope of the instant claims. Claim 1 is generic to all that is recited in claim 1 of US patent 6,849,249. That is, claim 1 falls entirely within the scope of claim 1 of the patent, or is anticipated thereby. The only difference is that patented claim 1 requires a Chrysamine a fluorophor moiety in the detectably-labeled compound, while instant claim 1 requires thioflavin derivative a fluorescent moiety in the detectably-labeled compound that binds to amyloid protein.

Conclusion

1. No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jagadishwar R. Samala whose telephone number is (571)272-9927. The examiner can normally be reached on 8.30 A.M to 5.00 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571)272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jagadishwar R Samala
Examiner
Art Unit 1618

sjr

VICKIE KIM
PRIMARY EXAMINER